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Inventors: David W. LEUNG et al. Docket No.: 077319-0383

 Trp GGGGACAGCCCCCACCATTCCTACCGCTATGGGCCCCAACCTCCCACTCC CACCTCCCTCCATCGGCCGGGCTAGGACACCCCCAAATCCCGTCGCCC CCTTGGCACCGACACCGACAGAGACAGACACACAGCCATCCGCCACCA CCGCTGCCGCAGCCTGGCGAGGGGGCCCAGCCCCCCAGGCCCCTAC CCA GGG GCA TGG GGAAGTCAGCAGGCGTTGGGGGGGGGGGGGGAATAGCGGCGGCAGC Pro Gly Ala Trp LGG Met Asp Leu TTGGATCCCTCTGAGGTGGCCAGA ATG 101 151 301 201 251 51

20 Н Phe CTG CTC TTC Leu Leu Leu Leu CTGCTGLeu Leu Phe TTCCTCCTGLeu Leu Leu CTG CTG 10 CIGMet 343

Lys AAG Ala CCC AGT GCC Ser Pro Ser AGC TGC CysPhe TTCLeu Trp TGG CIG Thr ACC Pro CCC Len CIGTG

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al.

Inventors: David W. LEUNG et Docket No.: 077319-0383

TTC TAC AAT GGC TGG ATC Asn Gly Trp Figure 1 (continued) Tyr Phe 40 CCC Ala Met AAG ATG LysPhe TTCPhe TTC

TAC

418

Tyr

C

Val GTG Ala g_{CC} Cys $_{
m LGL}$ Val GTG Pro CCTIle GCC ATC Leu Ala CTCVal GTG 50 Ala GCT Len CTGPhe $T^{T}C$ 455

Ц Arg 70 CGTLeu TTGIle ATC LysAAG Met ATG Asn AAC Glu GAG GTC Val Asn AAC Arg CGC G1yGGA 09 Arg CGA 493

Arg CGA Ile GGG ATC G1yTyrCTG TAC Leu TYrTACLysAAA Ile ATC His CAC Leu CICLeu CIGMet ATG TA530

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al.

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

CCC Pro CCIPro TTCPhe 1 (continued CAC His CAC His 90 GCTAla G1yFigure CGA GGG Arg Val GTG Glu GAG

GTG

568

Val

C

Ser

C

 ${
m TCG}$

Leu CTCSer $ext{LCL}$ Ser AGC Gln CAG His CAC Asn TCC AAC Ser Val GTC Val 100 GTTVal GTTTYr \mathtt{TAT} Pro CCC 605

 \mathcal{O} H Arg CGC 120 G1yCCC CCA Pro Leu CIGGTA Val GAG Glu Met ATG Met ATG G1yGGG ren ren CTT110 Asp 643

GGC Ala GCT Leu Trp $_{
m LCG}$ CTGGlu Leu CGC GAG CTA Arg LysAAG Ala SCC Ile ATTPro CCC Val GTGζS GI 680

130

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID **ACYLTRANSFERASE** Inventors: David W. LEUNG et al.

Docket No.: 077319-0383

Figure 1 (continued)

Д Е Ile ATC CTG GCA GGA GTC Val G1yTrp Leu Ala 140 TGG CysTGC Leu Ala GGG CTG GCC G1yCCC Ala TCT Ser 718

Val TC ATC GAC CGG AAG CGC ACG GGG GAT GCC ATC AGT GTC Ser Thr Gly Asp Ala Ile Lys Arg 150 Ile Asp Arg he 755

Gln Asp V G 170 GCC CAG ACC CTG CTC ACC CAG GAC Gln Thr Leu Leu Thr Ala Val GTC Glu TCT GAG Ser 160 Met ATG 793

TIT CCT GAG GGA ACG AGA AAC CAC Glu Gly Thr Arg Asn His ProPhe GTGVal AGG GTC TGG Trp Val Arg IG 830

180

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 1 (continued)

C 耳 TTCPhe CCC Lys Arg Gly Ala TTC AAA CGT GGC Phe 190 CCC Pro CTG Leu ATG Met $_{
m LCC}$ Ser CCC G1yAAT Asn 868

ATA Ile CCC Pro GTCVal ATTIle CCC Pro CAG GTT Val Gln CCC Gln Ala CAG 200 GTGVal GCA Ala CTTLen AT 1.S 905

C Ö 220 AAG LysAAG Lys TGC CysTAC Tyr TTCPhe GAC Asp CAA Gln TAC Tyr TCC Ser $_{
m LCC}$ Ser ATG Met GTCVal 943

GTGVal CCC Gln Val Arg GTGCAG GGA CAA TGT CysGly Gln ${
m TCG}$ Ser ACC Thr TTCPhe CGC Arg CGTArg AG lu 980

ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 1 (continued)

C K Asp ACG GAA GGG CTG ACA CCA GAT Pro. Glu Gly Leu Thr 240 Thr Pro CCC GLG Val Pro CCA CCC Pro CLCLeu 1018

TCC ATG Ser Met CGG CAC Leu Ala Asp Arg Val Arg His CCA GCT CTG GCT GAC AGA GTC 250 Pro Ala AC GTC Val 1055

 \mathcal{Q} Ö CGG 270 Thr Asp Gly Arg TTC CGG GAA ATC TCC ACT GAT GGC Ser Glu Ile Arg Phe GLLVal ACT Thr 260 CICLeu 1093

GT GGT GGT TAT CTG AAG AAG CCT GGG GGC GGT GGG TGA ACCCTGGCTCTGAGCTCTCCTCCCATCTGTCCCCATCTTCCTCCC CACACCTACCCAGTGGGCCCTGAAGCAGGGCCAAACCCTCTTCCTT GTCTCCCCTCTCCCCACTTATTCTCCTCTTTGGAATCTTCAACTTCTGAA ly Gly Gly Asp Tyr Leu Lys Lys Pro Gly Gly Gly 280 1130 1216 1266 1168

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 1 (continued)

GGAGTTGGGGAAAGGAACGAACCCTGGCTGGAGGGGATAGGAGGGCTTTTT	1966
1916 ACAAGGGGAAGAAGCAGACATCAGGTGCTGCACTCACTTCTGCCCCCTGG	1916
GACATGACCCCACCCAGCCCCTGCAGCCCTGCTGACCATCTCACCAGAC	1866
TCAGTCTCCACATTTCTGGTTTTTCTGTCCCCATAGTACAGTTCTTCAGTG	1816
GCCTGCCCTTGCCCAGATGCCCAGGGTCGTGCACTCTCTGGGATACCAGT	1766
TGTAGCCTCCTGTCAGTGGGGGCTGGACCCTTCTAATTCAGAGGTCTCAT	1716
CCCAGGCTCATCCTGGGAGCTTTCCTCAGCACCTTCACCTTCCCTCCC	1666
TGTGAGGAGGACTTCTCGCCCTCTGGCTGGAAGCTGATACCTGAAGCACT	1616
ACAAATCCCCCCCCACTCCAAAGTCCATGGATTCAATGGACTCATTT	1566
CTCTACCCCTCTACCCCCACATTGGCCAGTGGACTCATCCATTCTTTGGA	1516
AAGGGAGGGAACATTCCATCCCCAGTGGAGTCTCTTTCCTATGTGGTCTT	1466
TGTCTGTGGGACAGTTGCCTCCCCCTCATCTCCAGTGACTCAGCCTACAC	1416
ACTCTTGCCTCGGTGCAGTTTCCACTCTTGACCCCCCACCTCCTACTGTCT	1366
1316 GTGAATGTGGATACAGCGCCACTCCTGCCCCCTCTTGGCCCCCATCCAT	1316

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 1 (continued)

2216 AAAATAAAGAGAGAGAAAAAAAAAAA	2216
5 TTTTGCGTGGTTGTTTTTTATTATTATCTGGATAACAGCAAAAAAACTG	2166
2116 CCCACAACTGGGGAGGTAGGCTGGGAGCAAAAGGAGGAGGGTGGGACCCAG	2116
5 TTTCTTCCTGGTGGCATTAGCCACTCCCTGCCTCTCACTCCAGACCTGTT	2066
2016 AATTTATTTCTTTTTCTGTTGAGGCTTCCCCCTCTCTGAGCCAGTTTTCA	2016

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

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10 20 30 40					•
MDLWPGAWM		LOO -YGIRVEVRG MLGLDVK -FGLKVECRK WAGVKVQLHA	150 -VPI-AKREL VTAKKSL TVTV-GKKSL STLAVMKKSS	LTQDVRVWV- KKNKRALWV- KKRRISIWM- KDFPRPFWLA	LAVQAQVPIV LAQQGKIPIV AAIAAGVPII SAVSIMRDFY
10 MDLWPGAWMLLLLLLF 1 MSV-IGRFLY YLRSVL-VVL 1 MAILYIF 60 70 51 FYNGWILFLA VLAIPVCAVR 51 FY	40 LWFCSPSAKY C ILVCVFGSIY LIVNAIQAVL	RIMELHIKYE ARCFYHVMKE GHMFGRLAPE WLQLVWVVDW	7 - 1 LG - 1		240 MLPFKRGAFH MLPFKKGAFH -LPFKTGAFH VLIPRTKGFV
10 1 MDLWPGAWM- 1 MSV-IGRFLY 1 M 1 MAI 51 FYNGWILFLA 51 FYRRINRFLA 51 FYRRINRFLA 51 LWAGSAGLAC 151 LWA	30 LL-LLFLLPT AL-AG RL-IITVIYS PLGLLFLLSG	80 GRNVENMKIL GKQHLAQWIT PRNPKHVATF	130 SSLDLLGMME STLDIFMLGR NNYDMVTASN SDIDWL-IGW	180 IDRKRTGDAI LDRSKRQEAI IDRNNRTKAH LERS-WAKDE	230 T T ASQGLPAPRN
201 101 101 101 101 101 101 101 101 101	20 <u>LLL</u> LLF YLRSV <u>L-WYL</u> <u>LYIF</u> P <u>L</u> V <u>LWYL</u>	70 VLAIPVCAVR VIASILCTLI CLFS EL	120 -PYVVVSNHQ KPYIMIANHQ -NAIYIANHQ -NAIYIANHQ EHALIISNHR	170 WLAGVIE WEMALSGTYE WLTGNLL WEAEYLE	220 GS SEL RGL AKLLAAQEYA
	$\frac{10}{\text{MDLWPGAWM}}$ $\frac{\text{MSV} - \text{IGRFLY}}{\text{M}}$ $\frac{\text{M}}{\text{M}} $	60 FYNGWILFLA FYG FYRINRFLA	110 AHHF-PPSQ- VVGE-ENLAK PTDA-ESYG- DEETYRSMGK	160 LWAGSAGLAC KYVPFLG LWIPFFGQLY KFLPVIGWSM	210 -FPEGTRNHN -FPEGTRSYT -FPEGTRSRG LFVEGTRFTP
uman LPAAT coli LPAAT aize LPAAT aize LPAAT coli LPAAT aize LPAAT aize LPAAT aize LPAAT uman LPAAT coli LPAAT aize LPAAT aize LPAAT aize LPAAT uman LPAAT uman LPAAT coli LPAAT aize LPAAT coli LPAAT	ਜਜਜਜ	51 51 51 51	101 101 101 101	151 151 151 151	201 201 201 201 201
国水坪 风团大开 风互大狂 对国水坦	Human LPAAT Yeast LPAAT E.coli LPAAT Maize LPAAT	Human LPAAT Yeast LPAAT E.coli LPAAT Maize LPAAT	Human LPAAT Yeast LPAAT E.coli LPAAT Maize LPAAT	Human LPAAT Yeast LPAAT E.coli LPAAT Maize LPAAT	Human LPAAT Yeast LPAAT E.coli LPAAT Maize LPAAT

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 2 (continued)

		DED	· !			:	EGS	:	ERS I		•	•	•	•
300	VPALADR- IGEFAEK- VRELAAH-	MSEMPKSDED	G.*	$\underline{\underline{\mathbf{v}}}^{\star}$	400	•	NDVNTHNEGS	•	QA <u>ERS</u>	450	•	•	•	•
290	VPTEGLTPDD ISTENLTKDK IDVSQYGKDQ	VIHVRMKRHA 340	GDYLKKPGGG G* DTTLPPQ	REAAGK PIGR <u>P</u> VKSLL	390	•	NEPVPSVSIS	•	GVMHVFIMFS	440	•	•	•	•
280	GOCQURULPP GCMIVRILKP GLVIVEMLPP	MLRILKGQSS 330	KEIGYSPAIN	AELDKEVAE- ATGTFDEEIR	380	•	HDKKVNKKIK 1	•	FTAAGMALVT (430				
270	YCKKERRFTS VSPKYGVFNR INLNRLHN	IVPKDSPQPT 320	VRHSMLTV-F VRDQMVDT-L	CRSIMEQK-I AKDALLDKHL	370	•	AL0	•	QLLSTWRGVA	420	•	KKMH *		KKE*
260	PIWMSSYQDF PWWSNTSTL PWCWSTTSNK	PAIYD <u>TT</u> V		VSKWCKDIFV	360	•	AIEYA	•	FGAIEFFKWT	410	•	NS	•	SARAARNRV
	251 251 251	251	301	301		351	351	351	351		401	401	401	401
	Human LPAAT Yeast LPAAT E.coli LPAAT	Maize LPAAT	Human LPAAT Yeast LPAAT	E.coli LPAAT Maize LPAAT		Human LPAAT	Yeast LPAAT	E.coli LPAAT	Maize LPAAT		Human LPAAT	Yeast LPAAT	E.coli LPAAT	Maize LPAAT

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383

60	120	180	240	300	360	420	450 460 470 480 ccrcgggg grctrctrca tcaaccggca gcgctctragc	530 540
GCCGTGTCTG	CGAGTTCTAC	CTCGCTCGTC	CTGGTTCGTG	; CAGGCTGCAG	GATGGGCCTC	CTTCCTGGGG		TCAGGGAGAA CCTCAAAGTG
50	110	170	220 230	290	350	410	470	
TGGAGCTGTG	GCCGCGCGGC	CCGCCGTGGC	GAGAACATGA GCATCATCGG	GGGACCCGCG	TCCTGGACAT	GGGAGCTGCT	TCAACCGGCA	
30 40	100	160		280	330 340	390 400	460	520
TCGGGCGCCG GGCCGGGCCA	GTGCAGCTGA	TTCACGGTGT		TTCGAGGTGC	CGTCTCCAAC CACCAGAGCA	CTGCGTGCAG ATCGCCAAGC	GTCTTCTTCA	GAGCGCATGG
	90	150	210	270	330	390	450	510
	GCTGCTGCTG	CGCGCTGTGC	CCGGACGGTG	CGGGCTCCGC	CGTCTCCAAC	CTGCGTGCAG	CCTCGGGGGC	CGACCTGGGC
20	80	130 140	200	260	320	380	440	500
GGCGGCGCCG	TGCTGTTGCT	GCCAAGGTCG CCCTGTACTG	GCCACGGCGG	AGTACTTTTA	CCTGTGTCAT	TTCCGGAGCG	TCATCATGTA	CAGTGATGGC
10	70	130	190	250	310	370	430	490
GGAGCGAGCT	900	GCCAAGGTCG	TGCCTGCTGT	CGAAGCTTCA	GAGGCCCGTC	ATGGAGGTCC	CCCGTGGGCC	ACTGCCATGA

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

					•		•	
600 TAAGAAGGGC	660 CTCTTCCTTC	720 TTCACTTCAG GAACAGTCAC AGTGCAGGTG	780 CGTGGACACC	840 GGAGAACGGG	900 GGGCATGACC	960	1020 AGGAAGCCCC	1080 CAGCTGGACC
590	650	710	770	830	890	950	1010	1070
TGCTGCCTTT	CCGTGGTGTA	GAACAGTCAC	TCCCTGCGCT	AGACCCCCCA	GACCACGGCA	GAGGGGACTC	CCCGGGAAGC	GCAGGGGGCT
580 AATGGGGACC	640 CCCATCGTCC		760 GCGGCGGACG	820 CACATCTCCA	880 CAGTAGCCCA	940 AGGATGGGCA	1000 TCTCACTCAG	1060 GGTGTCCCCT
570	630	680 690	750	810	870	930	990	1050
TCGCAACGAC	GGCACAGGTG	ACAACACCAA GAAGAAGTTC	CGGCCTCACT	CACCTTCCTC	GCAGCCGGCC	CGATGGCTGG	CTCCCCCAGC	ACAGGCCCCT
560	620	680	740	800	860	920	980	1040
CCGAGGGTAC	TGGCAGTCCA	ACAACACCAA	TCCCCACCAG	CCATGAGGAC	GGTCTGGCGT	AGGTGGAAGC	CTCTGTCCGG	GGTCTCAGAC
550	610	670	730	790	850	910	970	1030
TGGATCTATC	GCCTTCTACC	TCCTCCTTCT	CTGGAAGCCA	TGCCACCGGG	GCCACTGCGG	TGGGGAGGGC	CCAAATACCA	TTCTGTCACT

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 3 (continued)

• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •		•		AAA
1440	1430	1420	1410	1400	1390
1380 AAAAAAAAA	1380 TCTTGGAAAA AAAAAAAAA AAAAAAAAA	1360 TCTTGGAAAA	1350 ATAAACACAC	1340 CTGTTTTTT	1330 TACTCCGTTG
1320 GTCAGCACTG		TGCTCCTGC TGGCCTGAAG AATCTGTGGG		1280 TCGGGGCCTG	1270 GAGCCGGGAA
1260 GGGCCACAGG		1230 1240 1250 GAGGCCAGGA GTCCCAGACT CACGCACCCT	1230 GAGGCCAGGA	1220 GGAGGACCCC	1210 GGAGCAGATG
1200 CGATGGCCCA	1180 1190 GGGCTGAGCC ACAAGGCCCC		1160 1170 TGCGGCTGTG GCCCGCTGGT	_	1150 AGATGAGGCT
1140 GGGNTGATAA	1120 1130 CCACGGCACC TCTGGGNGCT		1100 1110 TCGAGGGCAG GGACTCGCGC	1100 TCGAGGGCAG	1090 CTCCCGGGC

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LELING et al.

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 4

	CCG	Pro
20	TGG	Trp
	CTG	Met Glu Leu Trp Pr
	GAG	Glu
01	ATG	Met
10 20 30	GGAGCGAGCTGGCGGCGCCGTCGGGCCCGGGCCC ATG GAG CTG TGG CCG	

	CTG	Leu	20
	CAG	Gln	
	GTG	Val Gln	
90			
	CTG TTG CTG CTG CTG CTG	Leu	
	CTG	Leu	
80	CTG	Leu	
	TTG	Leu	
	CTG	Leu	
0 /	CTG	Leu	
	\mathfrak{SCG}	Ala	10
	BSS	a Ala Ala Leu 1	
	CCC	Ala	
09	CTG	Leu	
	TGT	Cys	

	r h	, n	
	909	•	
40	TGC	Cys	
ਜੋ	TAC	Tyx	
	CTG		
0	gcc	Ala	
130	GTC	Val Ala	30
	AAG	Lys	
	gcc	Ala	
120	TAC	Tyr	
	TTC	Phe	
	3AG	31n	
110) DD5 :	Ala	
—	CCG	Ala	
	CGC	Arg	
100	AGC	Ser	

	CTG	Leu	20
	CTG	Leu	
	TGC CTG (Cys	
180	GIO	Val	
	TCG CIC	Leu	
	TCG	Ser	
170	C GTG GCC T	Ala	
(-)	GTG	Val	
	ဗ	Al	
0.0	\mathbf{ICC}	Ser	
160	GTG TCC	Val	40
	ACG	Thr	
		Phe	·
150	1GC	Cys	
	CTG	Leu	

	ტ	Q	
		Trp	
230	၁၅၅	G1y	
0	ATC	Ile	
	ATC	Ile	
220	AGC	Met Ser	
22	ATG	Met	09
	AAC	Asn	
	GAG	Glu	
210	GTG GAG	Val	
	ACG	Thr	
	CGG	Arg	•
200	GGC	G1y	
.,	CGC	G1y	
	CAC	His	
90	TGC	Cys	
\vdash			

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

GTC Val 110

GAG Glu

360 CTC ATG (Leu Met (

GGC Gly

ATG Met

CTG

CAC His

TCC

350 GAC ATG A

340 CAG AGC ATC (

330 AAC

		JIG.	Val	80		GTC	al
			-			_	•
		GA(Glu		320	AT(ΪŢ
		TTC	Phe		(-,	GTC	Val Ile
	270	CGC	Arg			$_{\mathrm{TGT}}$	Cys
<u>-</u>		CTC	Leu		0]	CCC	Arg Pro
Figure 4 (continued)		GGG	Gly		310	CGT	Arg
nti	260	TAC	Tyr				Ala
<u>ပ</u> (ပ		TTT	Phe			GAG	Glu
e 4		TAC	Tyr		300	CAG	$_{ m Gln}$
igur	250		Lys				Leu
E	2.5	TTC	Phe	70		AGG	Arg
		AGC	Ser		290	CGC	Arg
			Arg		.,	SCG	Pro
	240	GTG	Val			GAC	Asp
		TTC	Phe		280	SSS	Arg

Val 110	TTC	TTC Phe 140	GAC Asp
Glu	.10 CTC Leu	TTC	500 GCC Ala
Met	410 CTG CTC Leu Leu	GTC Val	500 ATG GCC Met Ala
Ile Leu Asp Met Met Gly Leu Met Glu	GAG Glu	450 GGC Gly	GTG Val
$_{ m G1y}$	400 AAG CGG Lys Arg 120	GGG G1y	
Met	400 AAG CG Lys Ar 120	CTC	490 ATG ACA Met Thr 150
Met	GCC Ala	40 TAC	GCC Ala D
Asp	ATC	4 ATC ATG Ile Met	ACT Thr
Leu	390 CAG Z	ATC Ile	480 AGC Ser
Ile	GTG Val	ひょ	TCT Ser
Ser 100	TGC	430 GGC CT Gly Le 130	CGC
Gln	380 GAG CGC Glu Arg	CCC GTG Pro Val	470 CGG CAG (Arg Gln i
His	GAG Glu	CCC Pro	cGG Arg
Ser Asn His Gln Ser 100	CCG	420 GGG Gly	AAC Asn
Ser	370 CTT Leu	CTG	460 ATC / Ile /

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

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	TAT Tyr 170	AAG Lys	GTC Val 200	AAG Lys	GCC Ala 230
	ATC Ile	590 TTT Phe	ATC Ile	680 AAG Lys	GAA Glu
	TGG Trp	590 CCT TTT Pro Phe	CCC	ACC Thr	CTG
540	GTG Val	CTG	630 GTG Val	AAC Asn	720 GTG Val
	AAA Lys	CTG CTG Leu	CAG	670 TTC TAC Phe Tyr 210	CAG
	CTC	580 GAC CTG ASP Leu 180	GCA Ala	670 TTC TP Phe TY 210	GTG Val
530	AAC Asn	GGG G1y	620 CAG Gln	rcc Ser	710 ACA Thr
וט	GAG AAC Glu Asn	AAT Asn	GTC Val	TCC	710 GTC ACA Val Thr
	AGG Arg	570 GAC Asp	GCA Ala	660 TTC Phe	ACA Thr
0	ATG GTC Met Val	AAC Asn	610 TAC CTG Tyr Leu	TCC	700 TCA GGA Ser Gly '
52	ATG Met 160	CGC Arg	61 TAC TYr 190	TCT Ser	700 TCA GG Ser G 220
	CGC Arg	560 ACT Thr	TTC Phe	650 GTG TAC Val Tyr	ACT Thr
	GAG Glu	GGT G	GCC Ala	GTG Val	TTC
510	GGC Gly	GAG Glu	600 GGC Gly	GTG Val	690 TTC Phe
	CTG	550 CCC Pro	AAG Lys	640 CCC Pro	AAG Lys

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

continued)	760
Figure 4 (co	750
	770

Val Val GAC GTC Asp 240 909 909 Ala Ala /50 ACT CIC Leu AGC Ser ACC Pro 730

TCC Ser 260 His CAC 810 CTC (Leu TTCACC ' Thr CGG GCC ATG AGG ACC Thr Arg Met Ala 790 Arg 250 CAC His TGC Cys 780 ACC Thr GAC

CAG Gln GTG00C TCTSer 999 929 Ala Gly 850 Ala ' CCC 999 Gly 840 AAC Glu Asn GAG CCC CAG Pro Gln 830 ACC Thr Lys 820

CCCAGACCACGGCAGGGCATGACCTGGGGAGGGCAGGTGGAAGC 910 980 900 970 890 960 880 TAG 870 GCC CAG 1 Gln CCG

CCTCCCGGCTTCCAAATACCACTCTGTCCGG

CGATGGCTGGAGGATGGGCAGAGGGGGACT

950

940

930

990

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 4 (continued)

1120 1130 1140 1150 1160	1180 1190 1200 1210 1220	1240 1250 1260 1270 1280	1300 1310 1320 1330 1340	1360 1370 1380
GGACTCGCGCCCACGGCACCTCTGGGNGCTGGGNTGATAAAGATGAGGCTTGCGGCTGTG	GCCCGCTGGTGGCCTGAGGCCCCCCGATGGCCCAGGAGGAGGACCCC	GAGGCCAGGAGTCCCAGACTCACGCACCCTGGGCCCACAGGGAAGCCGGGAATCGGGGCCTG	CTGCTCCTGCTGAAAAATCTGTGGGGTCAGCACTGTACTCCGTTGCTGTTTTTT	ATAAACACTCTTGGAAAAAAAAAAAAAAAAAAAAAAAAA
1110	1170	1230	1290	1350

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 5

Alignment of LPAAT Sequences.

1	1 MAKTRUSS-L RNRRQLKP AVAATADD DKDGVFMV 1 MDASCASSFL RGRCLESCFK ASFGMSQPKD AAGQPSRRPA DADDFFTVDD	60 70 80 90 100	51 QLSRABE EYAKVAL-YC ALGFTVSAVA SLVCLLGGG RIVENM-SII		 	MLKL	 		51 DRWITVILSV VRIACFL- SMWITIWN MIMILLEWP YARIRGGNIX
Human LPAAT-β Human LPAAT-α Yeast LPAAT E.coli LPAAT H.influenzae	L.douglassi C. nucifera		Human LPAAT-β Haman LPAAT-«	.Yeast LPAAT	E.coli LPAAT	H. influenzae	S.typhimuriu	L.douglassi	C. nucifera

Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383

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110 120 130 140 150	101 GWFVRSF <u>KYFYGLRFEV RDPRRLQEAR PCVIVSNHQS ILDMNGIMEV</u>	ILHIKY LYGIRVEV RGAHHFPPSQ PYVVSNHQS SLDILGWMEV	-HVMKLMLGLOVKV VGEENLAK-K PYIMIANHQS TIDIEMCRI	FGRL APLFGLKVEC RKPTDAESYG NAIYIANHON NYDMVTASNI	FGRL-FT YPLFGLKVEH RIPODOKOIS RAIYIGNHON NYDMVTISYM	FGRL-FT APLFGLKVEC RKPADAENYG NAIYIANHON NYDMVTAANI	IGGLV IMIYGIPIKI QGSEHIKKRA IFT <u>yi</u> sahas pidaefvam	$\Gamma_{\overline{CR}}$ M. $\overline{L}_{\overline{CR}}$ M.	160 170 180 190 200	151 LPERCVOIAK REILFIGPVGLIMYLGGV FFINRORSST AMIVMAIL	RCV PIAK RELLWAGSA GLACWLAGV IFIDRKRTGD AIS - VMSEV	GCTVTAK KSLKWPFLGWFMALSGT YFLDRSKRQE ALD-TINKG	PIVITYCK KSLIMIPFFGOLYWLTCN ILIDRINKTK AHGTIAEV	RIVSVOK KSLIMIPFFF TGILYWVFON IFLDRENRTK AHN-TMSOL	PIVITYCK KSLLWIPFFF TGQLYWLTGN ILIDRINNRAK AHS-TIAAV	STVGVAK KEVIWYPILG Q—LYTLAH IRIDRSNPAA ALQSFIMKEA	STVT IAK KEIIWYPLEG OFFLYVLANH ORIDRSN PSA ALESIKEV
110	GWFVRSF KY -	RLMITHIKY-	CFY-HVMKL-	CHMFGRL	ARW FGRL -FT	GHMFGRL-FI	CHIIGAN	GHVI GRIM. FT	160	I.P ERCV () IAK	LP GRCV PIAK	F PP GCTVT AK	VOP PIWIWGK	VOPRIVSVGK	VOPPTVTVCK	APIGIVGVAK	1 PK TVT IAK
	101	101	101	101	101	101	101	101		151	151	151	151	151	151	151	151
	Human LPAAT-β	Human LPAAT-α	Yeast LPAAT	E.coli L.PAAT	H. influenzae	S.typhimuriu	L.douglassi	C. nucifera		Human LPAAT-β	Human LPAAT- α	Yeast LPAAT	E.coli LPAAT	H. influenzae	S.typhimuriu	L.douglassi	C. nucifera

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

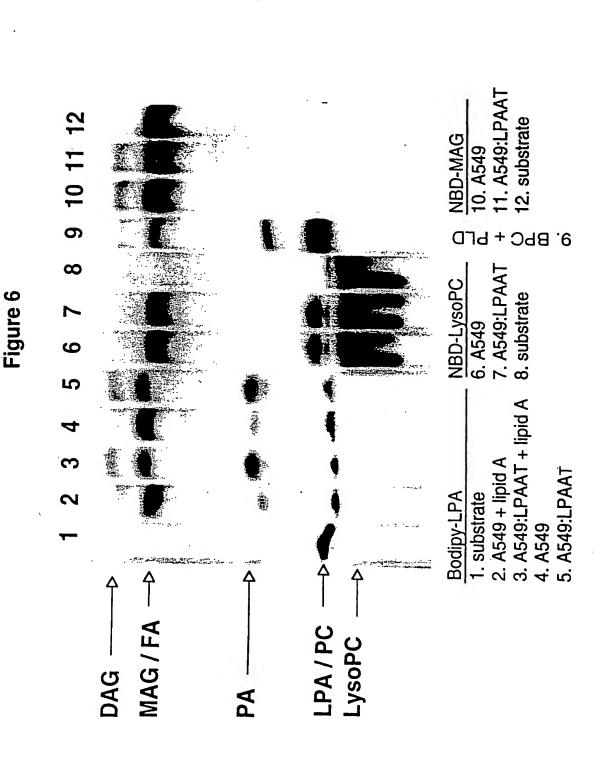
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210 220 230 240 250	201 GERMRENLK VWI YPEGTRN DNGDL-LPF KKGAFYL-A VQAQVPIVPV	ACTILITODAR VWVFPEGTRN HNGSMI.PF	LENVKKINKRA LWVFPEGTRS YTSELTMLPF	WHFKKRRIS	ARRINEDNIS IMMFPEGIRN RGRGL-LPF	WHFKKRRIS	201 VRVITEKNIS LIMFPEGIRS COGRL-LPF KKGFVHL-A LOSTLPIVPM	<u>ARAWKKNLS</u>	260 270 280 290 300	251 VYSSFS F YNTKKFFTS GIVIVOVLEA IPTSGLTAAD VPALVDICHR	251 VMSS YOD F YCKKERRETS GOOVRVLPP VPTEGLTPDD VPALADEVEH	251 WSNISTL VSPKYGVENR GOMIVRILKP ISTENLIKOK IGEFAEKVRD	251 CVSTTS NKINLARIHN GLVIVEMLPP IDVSQKGKDQ VRELAAHCR-	251 VCSSTH NKINLARWON GKVICEIMOP IDVSGYTKON VRDLAAYCHE	251 CVSNTS NKVNLNRINN GLVIVEMLPP VDVSEXGKDQ VRELAAHCRF	251 ILTGTHLAWF TRKGIFRVRP VPITVRYLPP INTDDMTVDK IDDYVKMTHD	251 VLTGTHLAWRKNSLRVRP APITVKYESP IKTDDWEEEK INHYVEMIHE
	Human L.PAAT-β	Human LPAAT-α	Yeast LPAAT	E.coli LPAAT	H.influenzae	S.typhimuriu	L.douglassi	C. nucifera		Human LPAAT-β	Human LPAAT- α	Yeast LPAAT	E.coli L.PAAT	H.influenzae	S.typhimuriu	L.douglassi	C. nucifera

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 5 (continued)

350 EPVPSVSI			•	•	•	•		•	•	•
330 340 350 3SGVQPAQ*		390	•		•			•		
330 SSGVQPAQ*- KKP G G G G* PPQALEYAAL	EATCKV*S-K*S-K* ASGRSNS*-	380			•	•	•	•	•	
KIPQENGATA GSGVQPAQ*- TDGRGGDVL KKPGGGG*- YSPAINDTTL PPQAIEYAAI	LDEELA KGN* LDKEVA - ER EATGKV* PLGSINR S-K* QKPLVSKGR DASGRSNS*	370			SSVKKMH*		•		-	
	TILMEKRIAE IDEEIA KGN*. TALMEOKIAE LDKEVA - ER EATGKV*- IYVRNILPASQ KPIGSTNR S-K* TALYVDHI.PE SQKPIVSKGR DASGRS NS*	360	1 1 1 1 1 1 1 1 1 1		SNDWITHNEG SS					
301	301 301 301 301 301		351	351	351	351	351	351	351	351
Human LPAAT-β Human LPAAT-α Yeast LPAAT	E.coil Lewil H.influenzae S.typhimuriu L.douglassi C. nucifera		Human L.PAAT-β	Human L.PAAT- α	Yeast LPAAT	E.coli LPAAT	H. influenzae	S.typhimuriu	L.douglassi	C. nucifera



Title: METHOD OF SCREENING COMPOUNDS THAT INHIBIT LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383

TLC Analysis of Acyltransferase Acitvity

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Induction of TNF in A549 LPAAT or A549 cells stimulated with mTNF and IL-1

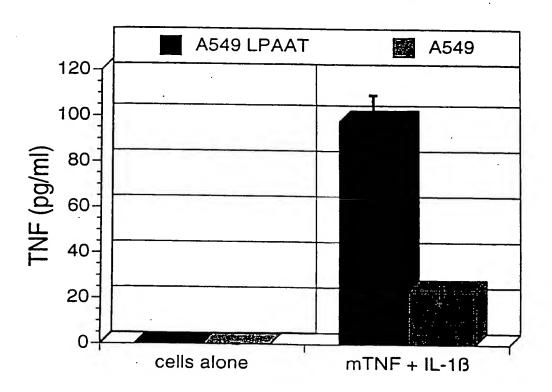


Figure 7

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Induction of IL-6 in A549 LPAAT or A549 cells stimulated with mTNF and IL-1

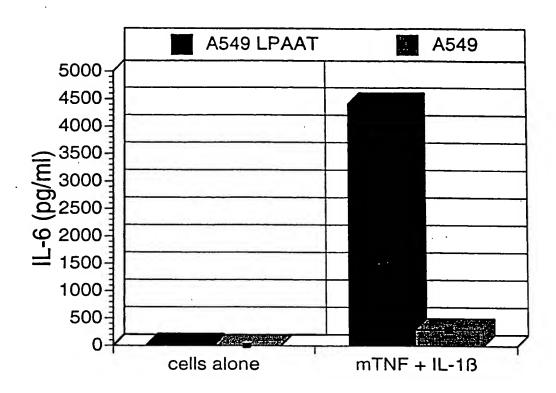
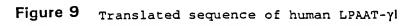


Figure 8

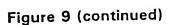
Inventors: David W. LEUNG et al. Docket No.: 077319-0383



TCTATGAAACCAACATACATGGCGTTTGCATCACAGTTGGAGTCAGATGTGAGCCCGGAG GGCAGGTGTCTGGCTTGTCCACCCGGAAGCCCTGAGGGCAGCTGTTCCCACTGGCTCTGC 120															
														120	
															180
GCC						TTC									225
	Met	GIA	Leu	Leu	_	Phe	Leu	Lys	Thr		Pne	Val	Leu	His	
					5					10					
						TTC									270
Leu	Leu	Val	Gly	Phe		Phe	Val	Val	Ser		Leu	Val	Ile	Asn	
15					20					25					
						CTG									315
Phe	Val	Gln	Leu	Cys		Leu	Ala	Leu	Trp		Val	Ser	Lys	Gln	
30					35					40					
						TGC									360
Leu	Tyr	Arg	Arg	Leu		Cys	Arg	Leu	Ala		Ser	Leu	Trp	Ser	
45					50					55			•		
						GAG									405
	Leu	Val	Met	Leu		Glu	Trp	Trp	Ser		Thr	Glu	Cys	Thr	
60					65					70					
						ACG									450
	Phe	Thr	Asp	Gln		Thr	Val	GLu	Arg		GIA	Lys	Glu	His	
75					80					85					
						CAC									495
	Val	Ile	Ile	Leu		His	Asn	Phe			Asp	Phe	Leu	Cys	
90					95					100					
						CGC									540
-	Trp	Thr	Met	Cys		Arg	Phe	GIY	Val		Gly	Ser	Ser	Lys	
105					110					115					_
						CTG									585
	Leu	Ala	Lys	Lys		Leu	Leu	Tyr	Val		Leu	Ile	Gly	Trp	
120					125					130					
						ATT									630
	Trp	Tyr	Phe	Leu		Ile	Val	Phe	Cys		Arg	Lys	Trp	Glu	
135					140					145					
						GTC									675
	Asp	Arg	Asp	Thr		Val	GIU	GIA	Leu		Arg	ren	Ser	Asp	
150					155		O.T.O.	C.T.C	m > 0	160	010				500
TAC	CCC	GAG	TAC	ATG	TGG	TTT	CTC	CTG	TAC	TGC	GAG	GGG	ACG	CGC	720
_	Pro	GIU	ıyr	Mec		Phe	reu	Leu	TYL		GIU	GIA	Thr	Arg	
165					170	000	C TTTT	300	» mc	175	CEC	000	m		265
						CGC									765
	Thr	GIU	Thr	гдг		Arg	Val	ser	Mec		Val	Ala	Ala	Ala	
180			com	CMC	185	220	mac	CAC	CTC	190		CCC	3.00		010
AAG	GGG	CTT	CCT	GIC	CIC	AAG	TAC	Uic	Tou	t au	רכפ	2	ACC	AAG	810
	GIY	Leu	Pro	Val		Lys	TAT	urs	Leu	205	PIO	Arg	THE	гĀ2	
195		100	3.00	CCA	200	AAG	mcc	CTC	ccc		202	CMC	CCX	CCE	055
GGC	TTC	ACC	ACC	31a	616	AAG	Cuc	tou	7~~	C1	ML~	UL-1	BCA	GCT	855
	Phe	Thr	THE	Ala	215	Lys	Cys	reu	ALG	220	inr	vai	Ala	Ala	
210		~ · ·	cm a	200		220	mm/C	707	CCA		220	* * C	CCC	mcc.	000
						AAC									900
	Tyr	Asp	Val	THE		Asn	Pne	Arg	GIY		ьys	ASI	Pro	ser	
225				cmc	230	~~~	220	220	ma c	235	CCC	~~~	3 000		0.45
CTG	CTG	GGG	ATC	CTC	TAC	GGG	AAG	AAG	TAC	GAG	600	GAC	ATG	TGC	945
	Leu	GIA	TTE	Leu		Gly	rys	rÅg	TYT		Ala	Asp	met	cys	
240					245	C 2 2	CAC	N mc	000	250	C 3 C				222
						GAA									990
	Arg	Arg	Pne	Pro		Glu	ASP	rre	Pro		Asp	GIU	гĀг	Glu	
255					260		CMC	ma ~	C 3 C	265		a	~~~	000	
GCA	GCT	CAG	TGG	CTT	CAT	AAA	CIG	TAC	CAG	GAG	AAG	GAC	GCG	CTC	1035

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

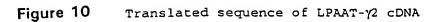




Ala 270	Ala	Gln	Trp	Leu	His 275	Lys	Leu	Tyr	Gln	Glu 280	Lys	Asp	Ala	Leu	
CAG	GAG	ΔΤΔ	тат	ТАА		AAG	GGC	ATG	TTT	CCA	GGG	GAG	CAG	TTT	1080
Gln	Glu	Tla	T3/2	Asn	Gln	Lys	Glv	Met	Phe	Pro	Glv	Glu	Gln	Phe	
285	Gru	116	171		290	-1-	1	-		295				E	
AAG	CCT	ccċ	ccc	AGG		TGG	ACC	CTC	CTG	AAC	TTC	CTG	TCC	TGG	1125
AAG	CCI	31-	2	700	D~0	Trp	The	Len	Len	Asn	Phe	T.eu	Ser	Trn	
300			_		305					310					
GCC	ACC	ATT	CTC	CTG	TCT	CCC	CTC	TTC	AGT	TTT	GTC	TTG	GGC	GTC	1170
Ala	Thr	Ile	Leu	Leu	Ser	Pro	Leu	Phe	Ser	Phe	Val	Leu	Gly	Val	
315					320					325					
TTT	GCC	AGC	GGA	TCA	CCT	CTC	CTG	ATC	CTG	ACT	TTC	TTG	GGG	$ extbf{T} extbf{T}$	1215
Phe	Ala	Ser	Gly	Ser	Pro	Leu	Leu	Ile	Leu	Thr	Phe	Leu	Gly	Phe	
330			_		335					340					
GTG	GGA	GCA	GCT	TCC	TTT	GGA	GTT	CGC	AGA	CTG	ATA	GGA	GTA	ACT	1260
Val	Glv	Ala	Ala	Ser	Phe	Gly	Val	Arg	Arg	Leu	Ile	Gly	Val	Thr	
345	4	•			350	_				355					
GAG	ATA	GAA	AAA	GGC	TCC	AGC	TAC	GGA	AAC	CAA	GAG	TTT	AAG	AAA	1305
Glu	Ile	Glu	Lvs	Gly	Ser	Ser	Tyr	Gly	Asn	Gln	Glu	Phe	Lys	Lys	
360			-	_	365		_			370					
AAG	GAA	TAA	TTA	ATGG	CTGT	GACT	GAAC.	ACAC	GCGG	CCCT	GACG	GTGG	TATC	CAGTT	1362
Lvs	Glu	***													
AAC'	TCAA	AACC	AACA	CACA	GAGT	GCAG	GAAA	AGAC.	AATT.	AGAA	ACTA	$\mathbf{T}\mathbf{T}\mathbf{T}\mathbf{T}$	TCTT.	ATTAA	1422
CTG	GTGA	CTAA'	TATT.	AACA.	AAAC'	TTGA	GCCA.	AGAG	TAAA	GAAT	TCAG	AAGG	CCTG	TCAGG	1482
TGA	AGTC'	TTCA	GCCT	CCCA	CAGC	GCAG	GGTC	CCAG	CATC	TCCA	CGCG	CGCC	CGTG	GGAGG	1542
TGG	GTCC	GGCC	GGAG.	AGGC	CTCC	CGCG	GACG	CCGT	CTCT	CCAG	AACT	CCGC	TTCC	AAGAG	1602
GGA	CCTT'	TGGC'	TGCT	TTCT	CTCC'	TTAA	ACTT.	AGAT	CAAA	$\mathbf{T}\mathbf{T}\mathbf{T}\mathbf{T}$	AAAA	AAAA	AAAA	AAA	1660



ACYLTRANSFERASE Inventors: David W. LEUNG et al. Docket No.: 077319-0383



AATTATGCGGCACCCATACAGGGACCCTCTGCGGCCATCATGGAGAGCCTTCATCTTGCC													61 121 181 238		
CTG Leu	GAG Glu	TGG Trp 5	TGG Trp	TCC Ser	TGC Cys	ACG Thr	GAG Glu 10	TGT Cys	ACA Thr	CTG Leu	TTC Phe	ACG Thr 15	GAC Asp	CAG Gln	283
		Val					Lys					Ile	ATC Ile		328
													ATG Met		373
GAG Glu	CGC Arg	TTC	GGA Gly	GTG Val	CTG Leu	GGG Gly	AGC	TCC Ser	AAG Lys	GTC Val	CTC Leu	GCT	AAG Lys	AAG Lys	418
		CTC					ATC					TAC	TTT Phe		463
		GTG					AAG						GAC Asp		508
GTG Val	GTC Val	GAA	GGG Gly	CTG Leu	AGG Arg	CGC Arg	CTG	TCG Ser	GAC Asp	TAC Tyr	CCC Pro	GAG	TAC Tyr	ATG Met	553
TGG Trp	TTT Phe	CTC	CTG Leu	TAC Tyr	TGC Cys	GAG Glu	GGG	ACG Thr	CGC Arg	TTC Phe	ACG Thr	GAG	ACC Thr	AAG Lys	598
CAC His	CGC Arg	GTT	AGC Ser	ATG Met	GAG Glu	GTG Val	GCG	GCT Ala	GCT Ala	AAG Lys	GGG Gly	CTT	CCT Pro	GTC Val	643
CTC Leu	AAG Lys	TAC	CAC His	CTG Leu	CTG Leu	CCG Pro	CGG	ACC Thr	AAG Lys	GGC Gly	TTC Phe	ACC	ACC Thr	GCA Ala	688
GTC Val	AAG Lys	TGC	CTC Leu	CGG Arg	GGG Gly	ACA Thr	GTC	GCA Ala	GCT Ala	GTC Val	TAT Tyr	GAT	GTA Val	ACC Thr	733
CTG Leu	AAC Asn	TTC	AGA Arg	GGA Gly	AAC Asn	AAG Lys	AAC	CCG Pro	TCC Ser	CTG Leu	CTG Leu	GGG	ATC Ile	CTC Leu	778
TAC Tyr	GGG Gly	AAG	AAG Lys	TAC Tyr	GAG Glu	GCG Ala	GAC	ATG Met	TGC Cys	GTG Val	AGG Arg	AGA	TTT Phe	CCT Pro	823
CTG Leu	GAA Glu	GAC	ATC Ile	CCG Pro	CTG Leu	GAT Asp	GAA	AAG Lys	GAA Glu	GCA Ala	GCT Ala	CAG	TGG Trp	CTT Leu	868
CAT His	AAA Lys	CTG	TAC Tyr	CAG Gln	GAG Glu	AAG Lys	GAC	Ala	CTC Leu	CAG Gln	GAG Glu	ATA	TAT Tyr	AAT Asn	913
CAG Gln	AAG Lys	GGC Gly	ATG Met	TTT Phe	CCA Pro	GGG Gly	GAG	CAG	TTT Phe	AAG Lys	CCT Pro	GCC	CGG Arg	AGG Arg	958
CCG Pro	TGG Trp	Thr	CTC Leu	CTG Leu	AAC Asn	TTC Phe	CTG Leu	TCC Ser	TGG Trp	GCC Ala	ACC Thr	ATT Ile	CTC Leu	CTG Leu	1003
TCT Ser	CCC Pro	245 CTC Leu	TTC Phe	AGT Ser	TTT Phe	GTC Val	250 TTG Leu	GGC Gly	GTC Val	TTT Phe	GCC Ala	255 AGC Ser	GGA	TCA	1048

Inventors: David W. LEUNG et al. Docket No.: 077319-0383





Figure 10 (continued)

260	265	270
CCT CTC CTG ATC CTG ACT TTC		
Pro Leu Leu Ile Leu Thr Pho	e Leu Gly Phe Val Gly	Ala Ala Ser
275	280	285
TTT GGA GTT CGC AGA CTG ATA		
Phe Gly Val Arg Arg Leu Ile	e Gly Val Thr Glu Ile	Glu Lys Gly
290	295	300
TCC AGC TAC GGA AAC CAA GAG		
Ser Ser Tyr Gly Asn Gln Gl	u Phe Lys Lys Lys Glu	***
305	310	
TGTGACTGAACACACGCGGCCCTGACG		
AGTGCAGGAAAAGACAATTAGAAACTA		
AACTTGAGCCAAGAGTAAAGAATTCAG		
AGCGCAGGGTCCCAGCATCTCCACGCC		
TCCCGCGGACGCCGTCTCTCCAGAAC		GGCTGCTTTCTC 1485
TCCTTAAACTTAGATCAAATTTTAAAA	AAAAAAAAAA	1523

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Figure 11 Translated sequence of human LPAAT- δ

тсаа	CCCA	GCCG	GCTC	ראתכי	rcago	CTTC	rggr	PTCT	AAGTO	ገሮልጥር	ንጥርርር	מממי	CCTC	CCAG	61
GAAG	GAGA		TTCC'	TGAG	CCT	GGAT	CTTTC	TTC	TTC	rggaz	ATCI	PTTG2	CTGT	CCAG	121
TAGT	TATT'	TATT	TCTG.	ATAA	AGAG	CGTC	CACG	CATC	ATG	GAC	CTC	GCG	GGA	CTG	175
					-							Ala			
CTG	AAG	TCT	CAG	TTC	CTG	TGC	CAC	CTG	GTC	TTC	TGC	TAC	GTC	TTT	220
			10	Phe				15				_	20		
ATT	GCC	TCA	GGG	CTA	ATC	ATC	AAC	ACC	ATT	CAG	CTC	TTC	ACT	CTC	265
			25	Leu				30					35		
CTC	CTC	TGG	CCC	ATT	AAC	AAG	CAG	CTC	TTC	CGG	AAG	ATC	AAC	TGC	310
			40	Ile				45					50	•	
AGA	CTG	TCC	TAT	TGC	ATC	TCA	AGC	CAG	CTG	GTG	ATG	CTG	CTG	GAG	355
			55	Cys				60					65		
TGG	TGG	TCG	GGC	ACG	GAA	TGC	ACC	ATC	TTC	ACG	GAC	CCG	CGC	GCC	400
			70	Thr				75					80		
				GGG											445
		_	85	Gly				90					95		
AAG	TTT	GAA	ATT	GAC	TTT	CTG	TGT	GGC	TGG	AGC	CTG	TCC	GAA	CGC	490
			100	Asp				105					110	_	
TTT	GGG	CTG	TTA	GGG	GGC	TCC	AAG	GTC	CTG	GCC	AAG	AAA	GAG	CTG	535
			115	Gly				120				_	125		
				ATT											580
	_		130	Ile				135					140		
				CGC											625
		_	145	Arg				150			_		155		
ACC	AGT	TTG	CAG	CAC His	CTC	7 ~~	ACD	TAC	Bro	GAG	AAG	TAT	TTT	TTC	670
			160	GAG				165					170		
CIG	TIO	CAC	CVC	Glu	Clv	Thr	A = a	Dhe	Thr	Clu	AAG	AAG	CAT	GAG	715
neu	TIE	птъ	175	Giu	GTA	1111	nr 9	180	1111	GIU	гуз	гÃг	185	GIU	
ATC	AGC	ATG		GTG	GCC	CGG	GCC		GGG	CTG	CCT	CGC		AAG	760
Ile	Ser	Met	Gln 190	Val	Ala	Arg	Ala	Lys	Gly	Leu	Pro	Arg	Leu 200	Lys	
CAT	CAC	CTG	TTG	CCA	CGA	ACC	AAG	GGC	TTC	GCC	ATC	ACC	GTG	AGG	805
				Pro											
AGC	TTG	AGA	AAT	GTA	GTT	TCA	GCT	GTA	TAT	GAC	TGT	ACA	CTC	AAT	850
			220	Val				225					230		
				GAA											895
			235	Glu				240					245	•	
AAG	AAA	TAC	CAT	GCA	GAT	TTG	TAT	GTT	AGG	AGG	ATC	CCA	CTG	GAA	940
_			250	Ala				255					260		
GAC	ATC	CCT	GAA	GAC	GAT	GAC	GAG	TGC	TCG	GCC	TGG	CTG	CAC	AAG	985
Asp	Ile	Pro	Glu 265	Asp	Asp	Asp	Glu	Cys 270	Ser	Ala	Trp	Leu	His 275	Lys	

Inventors: David W. LEUNG et al. Docket No.: 077319-0383

Figure 11 (continued)

	TAC Tyr														1030
	ACC Thr														1075
	CTC Leu													CCT Pro	1120
_	TTC Phe														1165
	CTG Leu														1210
	CGA Arg														1255 366
	GGC Gly												CTC	AGGG	1301
AGGTO GGGAO CCAGO	CACG	STGAC	AAA:	GCT	GGT	GAGC	CCT	GCTG	GCA	CGGC	GGAA	GTCA	CGAC	CTCT	1361 1421 1481
TCCCC GTGTC GGGC	GTG	AGTGT	rgaa(CTTTC	STTC	rgtg <i>i</i>	ATCA	raga.	AAGG	TAT	ATTT	GGCT	GCAG	GGGA	1541 1601 1661
TGTA!														TATT	1721 1774

Inventors: David W. LEUNG et al. Docket No.: 077319-0383



Figure 12

	10	20	30	40	50
LPAAT-γ1	MGLLAFLKTQ	FVLHLLVGFV	FVVSGLVINF	VQ-LCTLALW	PVSKQLYRRL
LPAAT-Y2					
LPAAT-δ	MDLAGLLKSQ	FLCHLVFCYV	FIASGLIINT	IQ-LFTLLLW	PINKQLFRKI
	60	70	80	90	100
LPAAT-γ1	NCRLAYSLWS	QLVMLLEWWS	CTECTLFTDQ	ATVERFGKEH	AVIILNHNFE
LPAAT-γ2		MLLEWWS	CTECTLFTDQ	ATVERFGKEH	AVIILNHNFE
LPAAT-δ	NCRLSYCISS	QLVMLLEWWS	GTECTIFTDP	RAYLKYGKEN	AIVVLNHKFE
	110	120	130	140	150
LPAAT-Y1	IDFLCGWTMC	ERFGVLGSSK	VLAKKELLYV	PLIGWTWYFL	EIVFCKRKWE
LPAAT-Y2	IDFLCGWTMC	ERFGVLGSSK	VLAKKELLYV	PLIGWTWYFL	EIVFCKRKWE
LPAAT-δ	IDFLCGWSis	ERFGLLGGSK	VLAKKELAYV	PIIGWMWYFT	EMVFCSRKWE
	160	170	180	190	200
				FTETKHRVSM	-
LPAAT-γ1	EDRITTVEGL	DDI CDVDEVM	WELLYCEGTR	FTETKHRVSM	EVALAKGI.PV
LPAAT-γ2	EDROTVVEGL	GRI BUABEKA	FELTHCEGTR	FTEKKHEISM	OVARAKGI.PR
LPAAT-δ	ODKETVATSL	QHERDIFER.	I I BINCECIN	TEMMETON	Qvardarent.
	210	220	230	240	250
LPAAT-Y1				LNF-RGNKNP	
LPAAT-Y2	LKYHLLPRTK	GFTTAVKCLR	GTVAAVYDVT	LNF-RGNKNP	SLLGILYGKK
LPAAT-δ	LKHHLLPRTK	GFAITVRSLR	NVVSAVYDCT	LNF-RNNENP	Z LLGVLNGKK
	260	270	280	290	300
LPAAT-γ1	YEADMCVRRF	PLEDIPLDEK	EAAQWLHKLY	QEKDALQEIY	NQKGMFPGEQ
LPAAT-Y2	YEADMCVRRF	PLEDIPLDEK	EAAQWLHKLY	QEKDALQEIY	NQKGMFPGEQ
LPAAT-δ	YHADLYVRRI	PLEDIPEDDD	ECSAWLHKLY	QEKDAFQEEY	YRIGTFPETP
	310	320	330	340	350
LPAAT-Y1	FKPARRPWTL	LNFLSWATIL	LSPLFSFVLG	VFASGSPLLI	LTFLGFV
LPAAT-Y2	FKPARRPWTL	LNFLSWATIL	LSPLFSFVLG	VFASGSPLLI	LTFLGFV
LPAAT-δ	MVPPRRPWTL	VNWLFWASIJV	LYPFFQFLVS	MIRSGSSLTL	ASFILVF
	360				
LPAAT-γ1		IGVTEIEKGS			
LPAAT-Y2		IGVTEIEKGS			
LPAAT-δ	FVASVGVRWM	IGVTEIDKGS	AIGNSDSKQF	י רואם.	

Inventors: David W. LEUNG et al. Docket No.: 077319-0383



